



HAL
open science

Evaluation of the 4 diagnosis criteria proposed by the SMFM and the AFE foundation for amniotic fluid embolism in a monocentric population

A. Ponzio-Klijanienko, A. Vincent-Rohfritsch, A. Girault, C. Le Ray, F. Goffinet, M.-P. Bonnet

► To cite this version:

A. Ponzio-Klijanienko, A. Vincent-Rohfritsch, A. Girault, C. Le Ray, F. Goffinet, et al.. Evaluation of the 4 diagnosis criteria proposed by the SMFM and the AFE foundation for amniotic fluid embolism in a monocentric population. *Journal of Gynecology Obstetrics and Human Reproduction*, 2020, 49, pp.101821. 10.1016/j.jogoh.2020.101821 . hal-03492594

HAL Id: hal-03492594

<https://hal.science/hal-03492594>

Submitted on 7 Nov 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

EVALUATION OF THE 4 DIAGNOSIS CRITERIA PROPOSED BY THE SMFM AND THE AFE FOUNDATION FOR AMNIOTIC FLUID EMBOLISM IN A MONOCENTRIC POPULATION

A. Ponzio-Klijanienko¹ ; A. Vincent-Rohfritsch² ; A. Girault¹⁻³ ; C. Le Ray¹⁻³ ; F. Goffinet¹⁻³ ; M.-P. Bonnet⁴

1- Maternité Port-Royal, AP-HP, APHP. Centre-Université de Paris, Paris, France, www.materniteportroyal.fr

2- Institut Mutualiste Montsouris, Paris, France

3- Université de Paris, INSERM U1153, Equipe de recherche en Epidémiologie Obstétricale, Périnatale et Pédiatrique (EPOPé), Centre de Recherche Epidémiologie et Biostatistique Sorbonne Paris Cité (CRESS), Paris, France

4- Département d'anesthésie-réanimation, Maternité Trousseau, Assistance Publique Hôpitaux de Paris, Université Paris Sorbonne, Paris, France

1 OBJECTIVE

2 The Society of Maternal Fetal Medicine (SMFM) and the Amniotic Fluid Embolism
3 Foundation have recently proposed four diagnostic criteria for amniotic fluid embolism
4 (AFE): presence of (1) sudden cardiac arrest or both respiratory and hemodynamic collapse,
5 and (2) biological disseminated intravascular coagulopathy (DIC), and (3) absence of fever,
6 and (4) clinical onset during labor or within 30 minutes of delivery.

7 The objectives of our study were to describe the clinical presentation of women with a strong
8 suspicion of AFE and to assess the validity of the four criteria proposed for AFE definition.

9 MATERIAL AND METHODS

10 We performed a retrospective study including all patients with a strong suspicion of AFE who
11 delivered between 2006 and 2018 at the Port Royal maternity unit, Paris. Strong suspicion of
12 AFE was defined by a clinical presentation in favor of AFE associated with a biological
13 pattern and/or autopsy result supporting AFE. The mention of AFE in files was essential to
14 include the patients in our study. We estimated the incidence and mortality rate of AFE. Then,
15 the presence of each of the four diagnosis criteria of the SMFM score was described, as well
16 as the clinical and biological patterns.

17 RESULTS

18 Among the 54 140 women who delivered during the study period, 14 had a strong suspicion
19 of AFE (0.03%), accounting for 25.9/100 000 deliveries (95%CI (12.3-39.5/100,000)). All
20 women had biological tests or autopsy supporting the diagnosis of AFE.

21 Six of 14 patients (43%) presented with all the four diagnostic criteria of the SMFM
22 definition. All 14 women presented a hemodynamic collapse, but respiratory symptoms were
23 lacking in 8 patients (57%); 71% fulfilled the criterion of biological DIC, and all patients had
24 a clinical coagulopathy and a massive postpartum hemorrhage. Absence of fever was lacking

1 in three women. In addition, all patients presented premonitory symptoms such as
2 neurological disorders or irreversible and inaugural fetal bradycardia.

3 CONCLUSION

4 The four SMFM diagnostic criteria were present in less than half of the women with a strong
5 suspicion of AFE. We propose an alternative clinical and pragmatic definition to diagnose
6 AFE, which has to be validated in the future. Early diagnosis of AFE based solely on clinical
7 criteria can help clinicians anticipate the severity of the situation and optimize care.

8

9 INTRODUCTION

10

11 Amniotic fluid embolism (AFE) is a rare but severe and life-threatening complication of
12 delivery. The national experts committee of the French Confidential Enquiry into Maternal
13 Deaths identified AFE as the third cause of maternal death in France in 2010-2012,
14 accounting for 9.4% of all maternal deaths⁽¹⁾.

15 Its reported prevalence varies from 1/8 000 to 1/80 000 deliveries ⁽²⁻⁴⁾, and its incidence from
16 2/100 000 to 8/100 000 deliveries ⁽⁵⁻⁷⁾ with a mortality rate between 10 % and 60% ^(8,9). These
17 variations can be explained by methodological issues in the identification of AFE, caused by
18 the lack of consensual definition for diagnosis of AFE. AFE is suspected in the presence of a
19 hemodynamic collapse and an acute respiratory distress, and/or cardiac arrest, general
20 convulsion and massive hemorrhage with coagulopathy. Other non-specific symptoms such as
21 neurological prodromes or abnormal fetal heart rate have also been described. None of these
22 symptoms is considered pathognomonic, and consequently several differential diagnoses are
23 often mentioned. These include massive obstetric hemorrhage with disseminated intravascular
24 coagulation (DIC), severe pulmonary embolism, and septic, anaphylactic or cardiologic
25 shock.

1 A population-based study using the United States Nationwide Inpatient Sample with an AFE
2 diagnosis based on the International Classification of Diseases, and aiming at identifying
3 retrospectively false-positive diagnoses of AFE was performed between 1999 and 2008
4 ⁽¹⁰⁾. Among the 402 cases of AFE included, only 68% (276 cases) presented one of the
5 following criteria: cardiac arrest, hypotension with respiratory distress, seizure, coma, DIC or
6 other coagulation disorders, with 32 % of the cases with none of the usual symptoms. The
7 same method was used in 2012 among women extracted from the Canadian register ⁽¹¹⁾. Of
8 the 292 cases identified as AFE, only 120 (40%) presented one or more of the criteria
9 previously described.

10 Based on these finding, a working group of the Society for Maternal-Fetal Medicine (SMFM)
11 and the Amniotic Fluid Embolism Foundation proposed in 2016 ⁽¹²⁾, a diagnosis of AFE based
12 on four criteria: (1) cardiorespiratory arrest or both hypotension and respiratory compromise,
13 associated with (2) documented DIC according to the International Society for Thrombosis
14 and Hemostasis (ISTH) score, with (3) a clinical onset during labor or within 30 minutes of
15 delivery, in the (4) absence of fever during labor.

16

17 In 2018, Bonnet and al. reviewed all cases of women who died of AFE in France between
18 2007 and 2011 ⁽¹³⁾. Among the 36 women included in this study, only 58% presented with the
19 four SMFM criteria. The most frequently missing criterion was the documented biological
20 DIC.

21 The validity of these criteria has also been tested by Stafford and al. over 115 cases extracted
22 from the Amniotic Fluid Embolism Registry, between 2013 and 2017 ⁽¹⁴⁾. Charts were
23 reviewed by experts who confirmed 68 cases of AFE. Among them, only 79% of these
24 fulfilled the four diagnostic criteria of the SMFM and the Amniotic Fluid Embolism
25 Foundation.

1 The validity of these criteria has yet been tested in a population-based cohort with a strong
2 clinical suspicion of AFE.

3 Thus, the objective of our study was to apply the diagnosis criteria proposed by the SMFM in
4 a population of women who presented a strong suspicion of AFE during labor or delivery. In
5 addition, we described the clinical presentation of these women in order to identify other
6 clinical diagnostic criteria.

7

8

9

1 MATERIAL AND METHODS

2

3 This monocentric retrospective descriptive study included all patients who presented a strong
4 suspicion of AFE in Port Royal maternity unit, a French tertiary university materno-fetal
5 medicine center, between January 1st, 2006 and December 31st,2018.

6 Women with a strong suspicion of AFE were defined as women with a clearly mentioned
7 diagnosis of AFE in the charts by one of the clinicians, during the acute event, associated with
8 the positivity of biological tests (IGFBP-1 dosage in blood and/or in bronchoalveolar lavage
9 and presence of amniotic and fetal cells in the bronchoalveolar lavage) or an autopsy in favor
10 of an AFE diagnosis.

11

12 All files identified from the hospital database using a computerized cross-referenced database
13 with the words: “amniotic fluid embolism”, “cardiac arrest”, “hysterectomy” and “DIC” were
14 reviewed one by one. The files of women admitted in the intensive care unit were also
15 reviewed.

16

17 All the data were collected from the medical charts. The following baseline maternal
18 characteristics were collected: maternal age, body mass index (BMI), cardiovascular history,
19 parity. We also collected pregnancy and delivery characteristics: mode of conception
20 (spontaneous or assisted reproduction technology), type of pregnancy (singleton or multiple),
21 gestational age at delivery (in weeks), labor induction, abnormal fetal heart rate during labor,
22 delivery modalities (spontaneous vaginal delivery, operative delivery, cesarean delivery,
23 either in emergency or not, and indications of the cesarean delivery), duration between
24 membranes rupture and event, birthweight and newborn gender.

1 To describe the clinical presentation of AFE and its chronology, the premonitory signs and
2 their timing were collected. Premonitory signs included neurological signs (seizure,
3 confusion, agitation, fainting or anxiety and imminent death feeling), abnormal fetal heart
4 rate, respiratory signs (dyspnea, cough, shortness of breath), and atypical signs (nausea and/or
5 vomiting, arterial blood hypertension, skin rash, thoracic or abdominal pain).

6 The following symptoms were searched: a cardiorespiratory arrest or both hypotension
7 (systolic blood pressure <90 mmHg) and respiratory compromise (dyspnea, cyanosis or
8 peripheral capillary oxygen saturation < 90%), massive obstetric hemorrhage (defined as a
9 rapid blood loss >1000mL) and clinical coagulopathy. The clinical coagulopathy was defined
10 by a subjective perception by the obstetrician of an excessive blood fluidity, a bleeding
11 without clot. For the biological coagulopathy, items were specified as platelet count,
12 prothrombin time, and fibrinogen level. If any patient had fever, we searched for a biological
13 sepsis (C-Reactive protein > 6mg/L, white blood cell count > 10 G/L) in the medical files.

14
15 Components of management such as surgical care were recorded: hysterectomy, vascular
16 ligation, uterine suture, perineal suture; management of obstetrical hemorrhage and of organ
17 deficiencies: blood transfusion (type (red blood cells, platelets, fresh frozen plasma) and
18 quantities), administration of fibrinogen concentrate, recombinant factor seven activated,
19 tranexamic acid, use of catecholamine drugs (type and dose), orotracheal intubation and
20 artificial ventilation, extracorporeal life supporting system.

21 We also collected maternal outcomes such as maternal death, blood loss, length of stay and
22 organ failure. The timing when the clinicians in charge of the patient suggested or affirmed
23 the diagnosis was also collected.

1 We finally examined the results of IGFBP-1 dosage in plasma or bronchoalveolar lavage, the
2 presence of amniotic and fetal cells in the bronchoalveolar lavage, and autopsy reports for
3 maternal death to confirm our diagnosis of AFE.

4

5 First, we calculated the incidence of AFE among all the women who delivered in the Port
6 Royal maternity unit during the study period. Then we described maternal, pregnancy,
7 delivery and neonatal characteristics among the included women.

8

9 Finally we checked for the presence of the 4 SMFM and the Amniotic Fluid Embolism
10 Foundation criteria to our study population ⁽¹²⁾:

11 “These uniform diagnostic criteria must all be present and must include:

- 12 - Sudden onset of cardiorespiratory arrest, or both hypotension (systolic blood pressure
13 < 90mmHg) and respiratory insufficiency (dyspnea, cyanosis or peripheral capillary
14 oxygen saturation < 90%)
- 15 - Documented of DIC following appearance of these initial signs or symptoms, using
16 scoring system of Scientific and Standardization Committee on DIC of the
17 International Society for Thrombosis and Hemostasis (ISTH), modified for pregnancy.
18 Coagulopathy must be detected before important and severe bleeding which could
19 account for dilutional or shock-related consumptive coagulopathy.
- 20 - Clinical onset during labor or within 30 minutes of placenta delivery.
- 21 - No fever > 38°C during labor.”

22

23 According to the modified scoring system for DIC during pregnancy by the ISTH, a score > 3
24 is compatible with DIC in pregnancy ^(15,16):

- 25 - Platelets count > 100 000/mL = 0; < 100 000/mL = 1, < 50 000/ mL = 2

- 1 - Prolonged prothrombin time or international normalized ration < 25% increase = 0,
2 25-50% increase = 1, > 50% increase = 2
3 - Fibrinogen level > 2g/L = 0, < 2g/L = 1
4

5 RESULTS

6

7 Among the 54 140 deliveries during the study period, 14 women had a strong suspicion of
8 AFE: 0.03% (95% CI : (0.01-0.04%)) accounting for 25.9/100 000 deliveries (95% CI (12.3-
9 39.5/100,000)).
10

11 The characteristics of the population are presented in Table 1: 12 of 14 women delivered after
12 37 weeks of gestation, the two women who delivered before 37 weeks had a termination of
13 pregnancy for fetal indication (one at 29 weeks and one at 35 weeks).

14 None of the patients included had a planned cesarean delivery, 5 had a, emergency cesarean
15 delivery for fetal indication. Six patients had a spontaneous vaginal delivery.
16

17 All 14 patients presented a massive obstetric hemorrhage and a clinical DIC, which was
18 reported by the clinicians in the medical files (Table 2). An intrauterine balloon tamponade
19 was placed in 8 patients (57%), and 7 patients had a surgical hemostatic treatment (50%): 4
20 (28%) had a vascular ligation and 5 a hysterectomy (36%); among them, two patients had a
21 vascular ligation followed by an hysterectomy. Eight patients received catecholamine drugs
22 (57%). Four patients had an Extra-Corporeal Life Support (30%).
23

24 Among the 14 women who were diagnosed with AFE, only 6 (43%) had all four diagnostic
25 criteria of the SMFM and Amniotic Fluid Embolism Foundation (Table 3). One patient had

1 three of the four diagnostic criteria and 7 (50%) only two. The most frequent lacking criterion
2 was hemodynamic collapse associated with respiratory distress. All patients did have a
3 systolic blood pressure < 90 mmHg, but respiratory symptoms were lacking in 8 patients
4 (57%). Four patients (29%) presented a cardiac arrest. For the DIC score of the ISTH, only 10
5 patients had a score > 3 (71%). All patients presented clinical symptoms of AFE during labor
6 or within 30 minutes of delivery: four patients presented a clinical criterion of the SMFM
7 definition after delivery. Three women had a fever > 38.5°C, but none of them presented
8 biologic signs of sepsis (increase of C-Reactive protein or white blood cells count).

9
10 All 14 patients had premonitory signs: 10 patients (71%) presented premonitory neurological
11 symptoms, such as seizures, coma, fainting or sense of imminent death, occurring in a median
12 time of 87 min before clinical suspicion of AFE (min:3- max:180 min); 8 patients (57%)
13 presented with abnormal fetal heart rates such as bradycardia without uterine hypertonia or
14 maternal hypotension. The bradycardias were inaugural, sudden and irreversible.

15
16 Regarding maternal outcomes, ten patients (71%) were hospitalized in ICU for a median
17 length of stay of 10 days (2-40 days). Three patients were admitted in the post-operative room
18 for continuous monitoring during several days after delivery. Median duration of total
19 hospitalization was 16 days (5-41 days).

20 One patient (7%, 95% CI (0,2-33,9%)) died. This woman was admitted in the maternity unit
21 in a critical condition. Membrane rupture had occurred at home and she had had seizures
22 immediately. When she arrived at the maternity, she was in a coma and the fetus in extreme
23 bradycardia. The cervix being fully dilated, the obstetrician performed an immediate
24 instrumental extraction but the newborn died after delivery.

25 Concerning fetal outcomes, the median neonatal pH was 7.02 (6.67-7.22) with 5 pH (42%)

1 under 7.0. Three (21%) newborns were hospitalized in neonatal ICU.

2 All patients had biological signs in favor of AFE: 4 had a bronchoalveolar lavage containing
3 amniotic and fetal cells, and 10 had an increase plasmatic concentration of IGFBP-1. **The**
4 **diagnosis of AFE was confirmed by autopsy on the patient who died.**

5 DISCUSSION

6

7 Among the 14 women with a strong suspicion of AFE, only 4 had all 4 diagnostic criteria
8 proposed by the SMFM and the Amniotic fluid Embolism Foundation ⁽¹²⁾. **The most frequent**
9 **missing criteria were respiratory distress, followed by biological DIC. In contrast,**
10 **premonitory signs were observed in all women.**

11

12 **In this study, all cases of suspected AFE were reviewed. To ensure a good completeness of**
13 **the cases, identification was performed using a computerized database and a cross-reference**
14 **research, the hospitalizations in the Intensive Care Unit were also reviewed. We collected**
15 **detailed data from the medical charts, in particular the chronology of the events. We reviewed**
16 **all cases one by one so the description of the population and of received care is also reliable**
17 **and complete, with only one missing data regarding blood loss estimation.**

18 **This study has also some limitations. It is possible that cases of AFE were not diagnosed**
19 **because of less severe symptoms and absence of biological tests. However, the most severe**
20 **cases are included, as all the patients who were admitted to ICU for AFE were included. A**
21 **multicentric study would have allowed including more patients. Yet, the monocentric design**
22 **provides homogeneity in the diagnosis strategy and management of these severe cases.**

23

24 **Our study included all patients with a strong AFE suspicion at Port Royal maternity unit, with**
25 **a higher incidence than reported in literature ⁽⁵⁻⁷⁾. Several reasons could explain the observed**

1 AFE rate. Port Royal maternity unit is specialized in high-risk pregnancies. The risk factors
2 described in literature include age > 35 years (OR 1.9), induction of labor (OR 1.8), delivery
3 by caesarean section or forceps (OR 12, 6 and 8.6) and placenta previa (OR 3.5)^(4,17). Indeed,
4 half of the patients included were > 35 years versus 21.3% in the 2016 French National
5 Perinatal Survey, a representative sample of all deliveries in France⁽¹⁸⁾. Two thirds of women
6 had labor induction as compared with 22% in the 2016 National Perinatal Survey.
7 However, some of true AFE can be missing, since we kept only files with a strong and
8 immediate suspicion of AFE.

9
10 One patient died (7% IC 95% (0,2-33,9%)), which is much lower than usually reported in the
11 literature, with a mortality rate between 27 % to 60%^(8,9). Even if the sample size of our
12 study is too small to draw any conclusion on maternal mortality from AFE, it suggests an
13 adequate management of these patients.

14
15 All 14 patients had a systolic blood pressure < 90 mmHg but dyspnea or cyanosis or SpO2 <
16 90% were lacking in 8 patients (57%), including 2 women who had general anesthesia for
17 emergency cesarean delivery. Consequently, including respiratory distress as an obligatory
18 criterion for diagnosis definition of AFE is questionable.

19 In the study from Stafford et al., 79% of the charts classified as “AFE” fulfilled the 4
20 diagnostic criteria of the SMFM and the AFE Foundation⁽¹⁴⁾.

21 In a retrospective study on maternal death from AFE in France, Bonnet et al. reported that
22 only 58,3% of women who died from AFE had the 4 diagnostic criteria⁽¹³⁾. The diagnosis of
23 AFE in these patients was confirmed by autopsy. In this study, the most frequent lacking
24 criterion was the documented DIC. Because the extreme severity of these cases, this could be
25 explained by the impossibility to perform blood test during management at an early time.

1 Contrastingly in our study DIC was diagnosed in 71% of our patients, but only one died.
2 The definition of SMFM and the AFE Foundation proposed to use the ISTH score for the
3 diagnosis of disseminated intravascular coagulopathy. Yet the ISTH score is quite
4 controversial in literature regarding its relevance during the pregnancy. Erez and al. proposed
5 a modified DIC score which includes the relative contribution of each of these 3 criteria
6 associated with a weight for the diagnosis of DIC ⁽¹⁹⁾. Thrombocytopenia was the less
7 discriminant reference element and **hypofibrinogenemia was the strongest discriminant**
8 **element**. This modified DIC score was compared to the ISTH score in the study of Jonard and
9 al. among women who had a postpartum hemorrhage ⁽²⁰⁾. The Erez's score had a sensitivity of
10 78%, a specificity of 97% (p <0.01) while the ISTH score had a sensitivity of 31%, a
11 specificity of 99%. Therefore, the ISTH score is probably not the more relevant score in
12 pregnant women because of its poor sensitivity.

13 Although the DIC score was lacking in 4 of our patients, DIC was constantly clinically
14 suspected, as in the retrospective study on maternal death from AFE in France.

15 Another alternative to biological assessment would be to perform a thromboelastography or
16 thromboelastometry test. Compared with standard hemostasis testing, it has the advantage of
17 providing results within 10 minutes and might, therefore, be used to provide early AFE
18 diagnosis ^(21,22). **Additionally, these tests explored fibrinogenemia**. The hypofibrinogenemia is
19 a very good biological criterion ^(19,23), which can be used as quickly as the bed-side test of
20 coagulopathy can be realized, in a way to affirm our clinical diagnosis. **But a lot of maternity**
21 **units do not have this quick diagnostic test, which is very expensive to get.**

22

23 **All patients included in our study presented with premonitory symptoms. United Kingdom**
24 **Obstetric Surveillance System, also considers premonitory signs as diagnostic criteria in**
25 **opposition with the SMFM and the AFE Foundation definition (24). Similarly, in the cohort**

1 study of all cases of women who died of AFE in France between 2007 and 2011, 81% of
2 patients had premonitory symptoms distributed as follow : 47% of neurological symptoms,
3 38% of discomfort and near death anxiety and 22% with signs classified as atypical (nausea,
4 abdominal pain, vomiting) and 14% with inaugural fetal heart rate abnormalities ⁽¹³⁾. These
5 results suggest we could use premonitory symptoms as a definition criterion of AFE.

6

7 According to the SMFM and AFE foundation definition, fever during labor is a criterion
8 excluding an AFE diagnosis ⁽¹²⁾. However, most of laboring women in France have an
9 epidural analgesia, which is well-known to increase the risk of fever during labor⁽²⁵⁾.
10 Moreover, in case of TOP, the use of prostaglandins for cervical ripening is also known to be
11 associated with fever ⁽²⁶⁾. Thus, we consider that this criterion is questionable and could be
12 removed.

13 The use of biological tests for DIC as a diagnostic criterion is limited by variation in the
14 criteria of DIC definition and also by the success of blood sample performance. Therefore, we
15 suggest to take into account only the clinical coagulopathy instead of biologically confirmed
16 the DIC. Only clinical signs would be used as diagnosis criteria of AFE.

17 An alternative definition would include premonitory symptoms and replace biologic
18 coagulopathy by a clinical criterion of DIC or massive early clinical hemorrhage.

19

20

21 In conclusion, we could propose a pragmatic modified version of the SMFM and the AFE
22 Foundation definition, which would include only clinical criteria:

- 23 1. Premonitory signs included neurological signs (seizure, confusion, agitation, fainting
24 or anxiety and imminent death feeling), abnormal fetal heart rate, respiratory signs
25 (dyspnea, cough, shortness of breath), and atypical signs (nausea and/or vomiting,

- 1 arterial blood hypertension, skin rash, thoracic or abdominal pain).
- 2 2. Sudden hypotension (systolic blood pressure < 90mmHg) or sudden cardiorespiratory
- 3 arrest. Suddenness is a subjective criterion that involves a brutal hemodynamic
- 4 change.
- 5 3. Clinical early massive obstetric hemorrhage or clinical DIC
- 6 4. Clinical onset during labor or within 30 minutes of delivery

7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

This definition would have allowed to diagnose 100% of our patients. The early clinical diagnosis of AFE may help clinicians anticipating the severity of the situation and preparing for acute supportive care. These new diagnostic criteria need to be further validated in a larger prospective cohort of women with strong suspicion of AFE.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31

1. Les morts maternelles en France : mieux comprendre pour mieux prévenir. 5e rapport de l'Enquête nationale confidentielle sur les morts maternelles (ENCMM) 2010-2012. :231.
2. Morgan M. Amniotic fluid embolism. *Anaesthesia*. janv 1979;34(1):20-32.
3. Knight M, Berg C, Brocklehurst P, Kramer M, Lewis G, Oats J, et al. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. *BMC Pregnancy Childbirth*. 10 févr 2012;12:7.
4. Abenhaim HA, Azoulay L, Kramer MS, Leduc L. Incidence and risk factors of amniotic fluid embolisms: a population-based study on 3 million births in the United States. *Am J Obstet Gynecol*. juill 2008;199(1):49.e1-8.
5. Rath WH, Hoferr S, Sinicina I. Amniotic fluid embolism: an interdisciplinary challenge: epidemiology, diagnosis and treatment. *Dtsch Arzteblatt Int*. 21 févr 2014;111(8):126-32.
6. Fässler M, Zimmermann R, QuackLötscher KC. Maternal mortality in Switzerland 1995-2004. *Swiss Med Wkly*. 9 janv 2010;140(1-2):25-30.
7. Knight M, Tuffnell D, Brocklehurst P, Spark P, Kurinczuk JJ, UK Obstetric Surveillance System. Incidence and risk factors for amniotic-fluid embolism. *Obstet Gynecol*. mai 2010;115(5):910-7.
8. Tuffnell D, Knight M, Plaat F. Amniotic fluid embolism - an update. *Anaesthesia*. janv 2011;66(1):3-6.
9. Gist RS, Stafford IP, Leibowitz AB, Beilin Y. Amniotic fluid embolism. *Anesth Analg*. mai 2009;108(5):1599-602.
10. Kramer MS, Abenhaim H, Dahhou M, Rouleau J, Berg C. Incidence, risk factors, and consequences of amniotic fluid embolism. *Paediatr Perinat Epidemiol*. sept 2013;27(5):436-41.
11. Kramer MS, Rouleau J, Liu S, Bartholomew S, Joseph KS, Maternal Health Study Group of the Canadian Perinatal Surveillance System. Amniotic fluid embolism: incidence, risk factors, and impact on perinatal outcome. *BJOG Int J Obstet Gynaecol*. juin 2012;119(7):874-9.
12. Clark SL, Romero R, Dildy GA, Callaghan WM, Smiley RM, Bracey AW, et al. Proposed diagnostic criteria for the case definition of amniotic fluid embolism in research studies. *Am J Obstet Gynecol*. 2016;215(4):408-12.
13. Bonnet M-P, Zlotnik D, Saucedo M, Chassard D, Bouvier-Colle M-H, Deneux-Tharoux C, et al. Maternal Death Due to Amniotic Fluid Embolism: A National Study in France. *Anesth Analg*. 2018;126(1):175-82.

- 1 14. Stafford IA, Moaddab A, Dildy GA, Klassen M, Belfort MA, Romero R, et al. Evaluation of proposed criteria for research reporting
2 of amniotic fluid embolism. *Am J Obstet Gynecol.* 2019;220(3):285-7.
- 3 15. Erez O. Disseminated intravascular coagulation in pregnancy - Clinical phenotypes and diagnostic scores. *Thromb Res. mars*
4 *2017;151 Suppl 1:S56-60.*
- 5 16. Rabinovich A, Abdul-Kadir R, Thachil J, Iba T, Othman M, Erez O. DIC in obstetrics: Diagnostic score, highlights in management,
6 and international registry-communication from the DIC and Women's Health SSCs of the International Society of Thrombosis and
7 Haemostasis. *J Thromb Haemost JTH.* sept 2019;17(9):1562-6.
- 8 17. Kramer MS, Rouleau J, Baskett TF, Joseph KS, Maternal Health Study Group of the Canadian Perinatal Surveillance System.
9 Amniotic-fluid embolism and medical induction of labour: a retrospective, population-based cohort study. *Lancet Lond Engl.* 21 oct
10 2006;368(9545):1444-8.
- 11 18. Les Enquêtes Nationales Périnatales. EPOPé. Disponible sur: [http://www.xn--epop-inserm-ebb.fr/grandes-enquetes/enquetes-](http://www.xn--epop-inserm-ebb.fr/grandes-enquetes/enquetes-nationales-perinatales)
12 [nationales-perinatales](http://www.xn--epop-inserm-ebb.fr/grandes-enquetes/enquetes-nationales-perinatales)
- 13 19. Erez O, Novack L, Beer-Weisel R, Dukler D, Press F, Zlotnik A, et al. DIC Score in Pregnant Women – A Population Based
14 Modification of the International Society on Thrombosis and Hemostasis Score. *PLoS ONE.* 11 avr 2014;9(4). Disponible sur:
15 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3984105/>
- 16 20. Jonard M, Ducloy-Bouthors AS, Fourrier F. Comparison of Two Diagnostic Scores of Disseminated Intravascular Coagulation in
17 Pregnant Women Admitted to the ICU. *PloS One.* 2016;11(11):e0166471.
- 18 21. Crochemore T, Piza FM de T, Rodrigues R dos R, Guerra JC de C, Ferraz LJR, Corrêa TD. A new era of thromboelastometry.
19 *Einstein.* 2017;15(3):380-5.
- 20 22. Pujolle E, Mercier FJ, Le Gouez A. Rotational thromboelastometry as a tool in the diagnosis and management of amniotic fluid
21 embolism. *Int J Obstet Anesth.* 2019;38:146-7.
- 22 23. Charbit B, Mandelbrot L, Samain E, Baron G, Haddaoui B, Keita H, et al. The decrease of fibrinogen is an early predictor of the
23 severity of postpartum hemorrhage. *J Thromb Haemost.* févr 2007;5(2):266-73.
- 24 24. Knight M, Kurinczuk JJ, Tuffnell D, Brocklehurst P. The UK Obstetric Surveillance System for rare disorders of pregnancy. *BJOG*
25 *Int J Obstet Gynaecol.* mars 2005;112(3):263-5.
- 26 25. Thierrin L, Mercier F-J. Analgésie péridurale et fièvre lors du travail. /data/revues/03682315/00340005/423/ [Internet]. 9 mars 2008
27 [cité 24 janv 2020]; Disponible sur: <https://www.em-consulte.com/en/article/115390>
- 28 26. Foster J, Mauger AR, Christmas BCR, Thomasson K, Taylor L. Is prostaglandin E2 (PGE2) involved in the thermogenic response to
29 environmental cooling in healthy humans? *Med Hypotheses.* nov 2015;85(5):607-11.

30

Table 1: Characteristics of the study population. BMI: Body mass index; WG: Weeks of Gestation

Maternal Characteristics	AFE diagnosis N=14
Maternal age, median (extremes)	33 (29-46)
BMI (kg.m2)median (extremes)	21 (18-27)
Cardiovascular history, n (%)	1 (7%)
Parity > 1, n (%)	7 (50%)
Including Parity > 3, n (%)	2 (14%)
Nulliparity, n (%)	7 (50%)
Multiple pregnancy, n (%)	1 (7%)
Assisted reproductive techniques, n (%)	3 (21%)
Gestational age at delivery > 37 WG, n (%)	12 (85%)
Gestational age at delivery > 41 WG, n (%)	3 (21%)
Induction of labor, n (%)	9 (64%)
Artificial rupture of membranes, n (%)	6 (42%)
Mode of delivery, n (%)	
Spontaneous vaginal delivery	6 (42%)
Operative vaginal delivery	3 (21%)
Planned cesarean section	0
Emergency cesarean section	5 (36%)
Birthweight (g), median (extremes)	3265 (1900-4240)
Male Newborn	7 (50%)

Clinical Hemorrhage	AFE diagnosis N = 14
Clinical hemorrhage, n (%)	14 (100 %)
Blood loss median (mL)	2500 (1500-4000)
Hemoglobin (g/dL), median (extremes)	7.5 (4.9 – 9.3)
Use of Oxytocin, n (%)	8 (57 %)
Use of Sulprostone, n (%)	13 (93%)
Clinical DIC, n (%)	14 (100%)
Biological DIC	
Platelets count in /mm ³ , median (extremes)	65 550 (19 000- 146 000)
Pro-Thrombin time in %, median (extremes)	34% (7-79)
Fibrinogen in g/L, median (extremes)	0.4 (0-1.6)
Transfusion, n (%)	14 (100%)
Red cells, median (extremes)	9 (4-24)
Platelets pack, median (extremes)	1 (0-5)
Plasma packs, median (extremes)	8 (4-34)
Fibrinogen transfusion in g, median (extremes)	6 (3-13.5)

Table 2: Hemorrhage characteristics in our population. The clinical coagulopathy is a subjective item defined as an hemorrhage without clot, very fluid at an early stage of the hemorrhage diagnosed by the physicians in charge.

Diagnostic criteria for AFE from the SMFM	Presence of the criterion in cases of strong suspicion of AFE N =14
All 4 diagnostic criteria	6 (42.8%)
3 criteria	1 (7%)
2 criteria	7 (50%)
1. Sudden onset of cardiorespiratory arrest or both hypotension and respiratory compromise	6 (42.8%)
2. Documentation of biological DIC using the scoring system from the ISTH ≥ 3	10 (71.4%)
3. Clinical onset during labor or within 30 min of delivery of placenta	14 (100%)
4. No fever $> 38^{\circ}\text{C}$ during labor	11 (78.5%)

Table 3: Presence of the criteria of the definition proposed by the SMFM in our population.